What is claimed:

1. A process for preparing a multivesicular liposomal particle composition, the process comprising:

a) providing a volume of first emulsion by mixing a volume of a first aqueous phase and a volume of a volatile water-immiscible solvent phase, said solvent phase comprising at least one amphipathic lipid and at least one neutral lipid;

b) mixing and emulsifying said first emulsion and a volume of a second aqueous phase in a mixer to provide a volume of a second emulsion, said second emulsion comprising a continuous aqueous phase; and

c) removing the volatile water-immiscible solvent from the second emulsion to form a volume of multivesicular liposomal particle composition,

wherein all steps are carried out under aseptic conditions, and wherein all solutions are sterile filtered, and wherein the multivesicular liposomal particle composition is immediately suitable for administration into humans.

264/4.1

2. The process of claim 1, wherein the mixer is a dynamic or static mixer.

3. The process of claim 2, wherein the static mixer is of Kenics or Koch design.

4. The process of claim 3, wherein the first emulsion and second aqueous solution are passed through the mixer at a linear velocity of from about 100 cm/min to about 500 cm/min.

5. The process of claim 1, wherein the volume ratio of the first aqueous phase to the water-immiscible solvent phase is from about 0.33 to about 1.6.

6. The process of claim 1, wherein the volume ratio of the first emulsion to the second aqueous phase is from about 0.05 to about 0.5.

7. The process of claim 1, wherein the at least one amphipathic lipid is selected from the group consisting of phosphatidylcholines, phosphatidylethanolamines, sphingomyelins, lysophosphatidylcholines, lysophosphatidylethanolamines, are phosphatidylglycerols, phosphatidylserines, phosphatidylinositols, phosphatidic acids, cardiolipins, acyl trimethylammonium propane, diacyl dimethylammonium propane, stearylamine, and ethyl phosphatidylcholine.

8. The process of claim 1, wherein the at least one neutral lipid is selected from the group consisting of glycerol esters, glycol esters, tocopherol esters, sterol esters, alkanes and squalenes.

9. The process of claim 1, wherein the second aqueous phase further comprises at least one sugar.

10. The process of claim 1, wherein the second aqueous phase further comprises at least one amino acid.

11. The process of claim 1 further comprising primary filtration of the multivesicular liposomal particle composition.

12. The process of claim 11, wherein the ~~primary filtration~~ filtering comprises:

a) a first concentration of the multivesicular liposomal particle composition, resulting in a concentration increase of from 2-6 times; and

b) a buffer exchange, resulting in a pH of the multivesicular liposomal particle composition of between about 5 and about 8.

13. The process of claim 12, further comprising a second concentration step.

14. The process of claim 11, wherein ~~the~~ primary filtration is a carried out by cross-flow filtration with a hollow ~~fiber~~ filter.

15. The process of claim 14, wherein the ~~primary filtration~~ filtering is conducted at a transmembrane pressure of from about 0.1 psi to about 7 psi.

16. The process of claim 11, wherein the ~~primary filtration~~ filtering further comprises back pulsing with a back pulse volume and a retentate back pressure.

17. The process of claim 16, wherein the back pulsing is periodic.

18. The process of claim 17, wherein the back pulsing step occurs from about every 0.5 to about every 10 minutes.

19. The process of claim 18, wherein the back pulsing step occurs from about every 1 to about every 5 minutes.

20. The process of claim 16, wherein the back pulse volume is from about 0.01% to about 5% of initial primary filtration volume.

21. The process of claim 20, wherein the back pulsing volume is from about 0.1 to about 1.0% of initial primary filtration volume.

22. The process of claim 16, wherein the primary filtration is conducted at a retentate back pressure of from about 0 psi to about 10 psi.

23. The process of claim 1, further comprising potency adjustment of the multivesicular liposomal particle composition.

24. The process of claim 23, wherein the potency adjustment is carried out secondary filtration.

25. The process of claim 23, wherein the potency adjustment is carried out by decanting the multivesicular liposomal particle composition.

26. The process of claim 1, wherein said solvent removal comprises contacting the second emulsion with an inert gas flow.

27. The process of claim 26, wherein the solvent removal comprises a series of solvent removal steps, wherein the gas flow rate varies at different steps.

28. The method of claim 27, wherein a first solvent removal step is characterized by an inert gas flow rate which is less than that of a second step.

29. The method of claim 28, wherein the gas flow rate of the first solvent removal step is from about 20% to about 50% that of the second step.

30. The method of claim 27, wherein a first solvent removal step is characterized by an inert gas flow rate which is greater than that of a second step.

31. The method of claim 30, wherein the gas flow rate of the first solvent removal step is from about 120% to about 400% that of the second step.

32. The method of claim 28, further comprising a third solvent removal step, wherein the gas flow rate of the third solvent removal step is less than that of the second solvent removal step.

33. The process of claim 1, wherein the first aqueous phase comprises a physiologically active substance, and the multivesicular liposomal particle composition comprises an encapsulated physiologically active substance.

34. The process of claim 33, wherein the physiologically active substance is selected from the group consisting of antianginas, antiarrhythmics, antiasthmatic agents, antibiotics, antidiabetics, antifungals, antihistamines, antihypertensives, antiparasitics, antineoplastics, antitumor drugs, antivirals, cardiac glycosides, hormones, immunomodulators, monoclonal antibodies, neurotransmitters, nucleic acids, proteins, radio contrast agents, radionuclides, sedatives, analgesics, steroids, tranquilizers, vaccines, vasopressors, anesthetics, peptides, prodrugs and pharmaceutically acceptable salts of the same.

35. The process of claim 34, wherein the physiologically active substance is selected from cytarabine, insulin, paclitaxel, 5-fluorouracil, floxuridine, morphine, hydromorphine, dexamethasone, methotrexate, bleomycin, vincristine, vinblastine, IgF-1, bupivacaine and amikacin.

36. A method of scaling up an emulsification process, the method comprising:

emulsifying a first system of two immiscible phases with a first impeller having a first impeller blade diameter, in a first vessel having a first vessel diameter at a first impeller rpm defining a first impeller blade speed to yield a first emulsion having a first emulsion viscosity;

emulsifying a second system of two immiscible phases with a second impeller having a second impeller blade diameter in a second vessel having a second vessel diameter at a second impeller blade speed defining a second impeller rpm to yield a second emulsion having a second emulsion viscosity, wherein the second impeller blade speed is substantially the same as the first impeller blade speed, and wherein the ratio of the first impeller blade diameter to the first vessel diameter is substantially the same as the ratio of the second impeller blade diameter to the second vessel diameter; and

determining and applying a power input to the second emulsion required to substantially equate the second and first emulsion viscosities, wherein the volume of the second emulsion is at least 10 times the volume of the first emulsion.

37. The method of claim 36, wherein the two immiscible phases are an aqueous phase and a volatile water-immiscible solvent phase.

38. The method of claim 37, wherein the aqueous phase comprises a physiologically active substance.

39. The method of claim 37, wherein the solvent phase comprises at least one amphipathic lipid and at least one neutral lipid.

40. The method of claim 37, wherein the solvent phase comprises a physiologically active substance.

41. The method of claim 36, wherein the two immiscible phases are a water-in-oil emulsion and an aqueous phase.

42. The method of claim 36, wherein the emulsification is performed in a shear-type mixer.

43. A method of removing a volatile solvent from a solvent spherule-containing composition, the method comprising:

contacting a volume of a solvent spherule-containing composition with an inert gas flow in a series of solvent removal steps, wherein the gas flow has a flow rate that varies at different steps.

44. The method of claim 43, wherein a first solvent removal step is characterized by an inert gas flow rate which is less than that of a second step.

45. The method of claim 44, wherein the gas flow rate of the first solvent removal step is from about 20% to about 50% that of the second step.

46. The method of claim 43, wherein a first solvent removal step is characterized by an inert gas flow rate which is greater than that of a second step.

47. The method of claim 44, further comprising a third solvent removal step, wherein the gas flow rate of the third solvent removal step is less than that of the second solvent removal step.

48. The method of claim 1, wherein the volume of aseptic multivesicular liposomal particle composition.

49. A process for preparing a multivesicular liposomal particle composition, the process comprising:

a) providing a volume of first emulsion by mixing a volume of a first aqueous phase and a volume of a volatile water-immiscible solvent phase, said solvent phase comprising at least one amphipathic lipid and at least one neutral lipid;

b) mixing and emulsifying said first emulsion and a volume of a second aqueous phase in a mixer to provide a volume of a second emulsion, said second emulsion comprising a continuous aqueous phase; and

c) removing the volatile water-immiscible solvent from the second emulsion to form a volume of multivesicular liposomal particle composition,

wherein the multivesicular liposomal particle composition is sterilized before filling, and wherein the multivesicular liposomal particle composition is immediately suitable for administration into humans.

50. A multivesicular liposomal particle composition made by the process of claim 1.

51. The process of claim 23, wherein the volume of multivesicular liposomal particle composition is pooled and further processed by multiple batch processing.

Add B1

add D7